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Original Research Article

# Prescribing pattern and pharmacoeconomic analysis of antidiabetic drugs

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**ABSTRACT**

**Background:** Diabetes Mellitus is a worldwide growing problem causing threat to patient's health because of its association with various complications and comorbidities. It is a chronic disease requiring lifelong medication which further adds to the economic burden. The objective of this study was to evaluate the prescribing pattern and to do pharmacoeconomic analysis of prescribed antidiabetic drugs.

**Methods:** This observational cross sectional study was conducted for 12 months duration in Outpatient Pharmacy of tertiary care hospital. Prescriptions with antidiabetic drugs were captured and evaluation of prescribing pattern along with pharmacoeconomic analysis of antidiabetic drugs was done.

**Results:** A total of 611 prescriptions with antidiabetic drugs were analyzed. There were total 4034 drugs in all prescriptions with a mean of 6.6 drugs per prescription. 4.28% of drugs were prescribed by generic name and 58.9% of prescribed drugs were from essential drug list. Dual drug therapy was prescribed in maximum number of patients (42.2%) followed by monotherapy (28.8%). More commonly prescribed class of antidiabetic drugs was biguanides as monotherapy (n=119) and its combination with sulfonylureas was prescribed maximally among dual drug therapy (n=158). Cost of monthly therapy for antidiabetic drugs prescribed as monotherapy was least with Biguanides (₹ 98.89/ month) whereas combination of biguanides and thiazolidinediones was least expensive among dual drug therapy (₹ 216/ month).

**Conclusions:** Biguanides was the most common prescribed class of antidiabetic drugs among monotherapy and its combination with sulfonylureas was most prescribed as dual drug therapy and both of these therapies were economical.

**Keywords:** Antidiabetic drugs, Diabetes Mellitus, Pharmacoeconomic analysis, prescribing pattern, Prescription, WHO core indicators

## INTRODUCTION

Diabetes mellitus (DM) comprises a group of metabolic disorders that share the common phenotype of hyperglycemia.[1] According to International Diabetes Federation (IDF), there were estimated 1,027,911 deaths of adults due to diabetes in 2015 in India.[2] IDF estimated that 72.9 million people suffered from diabetes mellitus in 2017 and by 2045, that number is expected to grow to 134.3 million.[3]

A plethora of drugs is available for treatment of Diabetes mellitus (DM). This can lead to variation in the prescribing pattern of antidiabetic drugs. Prescribing pattern can also vary from one doctor to another depending on the lab results and association of DM with complications and comorbidities. Irrational prescription can lead to drug interactions, adverse drug reactions, failure of therapy which further adds up to healthcare costs. Periodic evaluation of prescribing pattern is beneficial in redefining guidelines as per current pattern of drug use.

The cost of drugs is the major deciding factor for the patient's compliance in case of DM as it usually requires lifelong treatment.[4] In today's time, many branded as well as generic drugs of same formulation of antidiabetic drugs are available in Indian market with significant variation in their costs.[4] Besides the lifelong treatment of diabetes, patients also need treatment for associated complications and comorbidities which leads to increase in economic burden on patient. India with a large population of people living with diabetes, spends an estimated USD 2.8 billion, or less than 1% of the global total on the prevention and treatment of DM.[5] Quality healthcare with minimum cost of therapy is need of the hour and keeping in view a large population suffering from DM and the economics involved, especially so in a developing country like India, this study was planned to analyse the prescribing pattern and pharmacoeconomic of antidiabetic drugs so as to take a step further in the rational use of drugs.

## METHODS

This cross sectional study was conducted in the Outpatient Pharmacy in Dayanand Medical College and Hospital, Ludhiana for a period of one year (January 1, 2017-December 31, 2017) for two days/ week. Informed consent waiver was given by Institutional Ethics Committee. There was an implied consent as patients had given the permission to photocopy his/her prescription. Prescriptions of all diabetic patients attending any outpatient department were captured and the data was entered in a proforma. Prescriptions of indoor patients were not included in the study.

***The following WHO prescribing indicators were used in the study[6]***

- Average number of drugs per encounter
- Percentage of drugs prescribed by generic name.
- Percentage of encounters with an antibiotic prescribed
- Percentage of encounters with an injection prescribed
- Percentage of drugs prescribed from essential drug list (updated National List of Essential Medicines 2015)[7]

In addition, Pharmacoeconomic analysis of the prescribed antidiabetic drugs was performed. An updated Current Index of Medical Specialities (CIMS) January-March 2017 edition[8] was used to note down the generic name and cost of various brands of antidiabetic drugs prescribed in OPD. Costs of prescribed antidiabetic drugs were taken into account and monthly cost analysis for each drug therapy was done. The data was entered in MS Excel 2007 worksheet and analysis was done using descriptive statistics. Data was described in terms of mean, frequencies and percentages as appropriate.

## RESULTS

Total of 611 prescriptions with antidiabetic drugs were collected from outpatient pharmacy. Evaluation of various variables such as age, weight and gender showed that the prevalence of diabetes mellitus was more in females (53.36%) as compared to males (46.64%). And maximum number of patients (35.02%) were in age group of 51-60 years followed by 61-70 years (23.40%).

Total number of prescribed drugs in all prescriptions was 4034 with average number of 6.6 drugs per prescription. Only 4.3% of drugs were prescribed by generic name and 58.9% of total prescribed drugs were from National List of Essential Medicines (NLEM). Antibiotics were prescribed in 7.8% of the prescriptions whereas injectables were prescribed in 25.5% of the total prescriptions (Table 1).

**Table 1: WHO core drug prescribing indicators.**

| Prescribing indicators | Value |
|---|---|
| Average number of drugs per encounter | 6.6 |
| Average number of antidiabetic drugs per encounter | 2.2 |
| Percentage of drugs prescribed by generic name | 4.3 |
| Percentage of encounters with an antibiotic prescribed | 7.8 |
| Percentage of encounters with an injection prescribed | 25.5 |
| Percentage of Essential drugs | 58.9 |
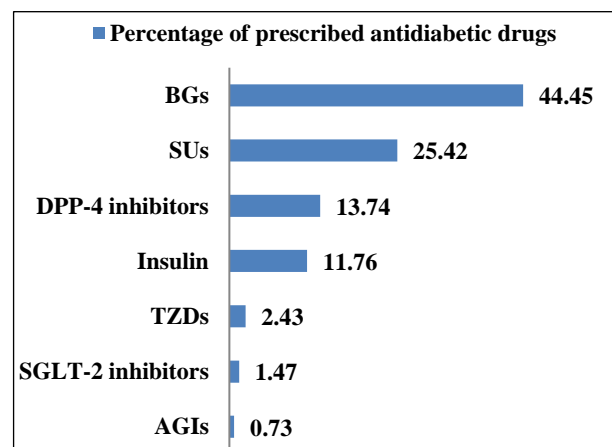


BGs: Biguanides, SUs: Sulfonylureas, DPP-4 inhibitors: Dipeptidyl peptidase-4 inhibitors, TZDs: Thiazolidinediones, SGLT-2 inhibitors: Sodium glucose co-transporter-2 inhibitors, AGIs-Alpha glucosidase inhibitors

**Figure 1: Class wise distribution of antidiabetic drugs (n=1361).**

Out of total 4034 prescribed drugs, 1361 were antidiabetic drugs with an average of 2.2 drugs per prescription. Biguanides constitute maximum share (44.45%) of total prescribed antidiabetic drugs followed by sulfonylureas (25.42%) (Figure 1).

Prescribed antidiabetic drug therapy ranges from monotherapy to six drug combination therapy. Dual drug therapy was most commonly prescribed (n=258) followed by monotherapy (n=176).

Biguanides were maximally prescribed as monotherapy (n=119) followed by insulin (n=42) whereas combined therapy of biguanides with sulfonylureas constitutes maximum share of dual drug therapy (n=158) followed by biguanides with insulin (n=42) and biguanides with Dipeptidyl peptidase-4 (DPP-4) inhibitors (n=34). Among dual drug therapy of biguanides with sulfonylureas, combination of metformin with glimepiride was more commonly prescribed followed by metformin combination with glipizide. Most commonly prescribed triple drug therapy was with biguanides, sulfonylureas and DPP-4 inhibitors (n=81) followed by biguanides with DPP-4 inhibitors and insulin (n=18). Combination of biguanides with sulfonylureas, DPP-4 inhibitors and Insulin constitutes maximum share of prescribed four drug therapy (n=11). Combination of biguanides with sulfonylureas, DPP-4 inhibitors, thiazolidinediones, insulin was the only five drug therapy prescribed to two patients.

Total of 372 Fixed dose combinations (FDCs) (37.92%) were prescribed. Two types of FDCs of antidiabetic drugs were prescribed: Two drug FDC (n=356) and three drug FDC (n=16)**.** Among two drug FDCs, biguanides with sulfonylureas was maximally prescribed (80.10% of total FDC) followed by FDC of biguanides with DPP-4

inhibitors (14.24%). Among three drug FDC, combination of biguanides, sulfonylureas and thiazolidinediones was maximally prescribed (3.23% of total FDCs) followed by combination of biguanides, sulfonylureas and alpha glucosidase inhibitors (1.08%) (Table 2).

### Table 2: Prescribing pattern of FDCs of antidiabetics (n=372).

| FDC of Antidiabetics | n (%) |
|---|---|
| BGs+SUs | 298 (80.10) |
| BGs+DPP-4 inhibitors | 53 (14.24) |
| BGs+AGIs | 1 (0.27) |
| BGs+TZDs | 4 (1.08) |
| BGs+SUs+TZDs | 12 (3.23) |
| BGs+SUs + AGIs | 4 (1.08) |

BGs: Biguanides, SUs: Sulfonylureas, DPP-4 inhibitors: Dipeptidyl peptidase-4 inhibitors, TZDs: Thiazolidinediones, AGIs- Alpha glucosidase inhibitors

Cost analysis of antidiabetic drug therapy revealed that average cost of antidiabetic drugs was ₹ 670.61/month per prescription. Minimum and maximum cost per prescription was ₹ 21.30 and ₹ 3847.80 per month respectively. Average monthly cost of all therapies were calculated (Figure 2).
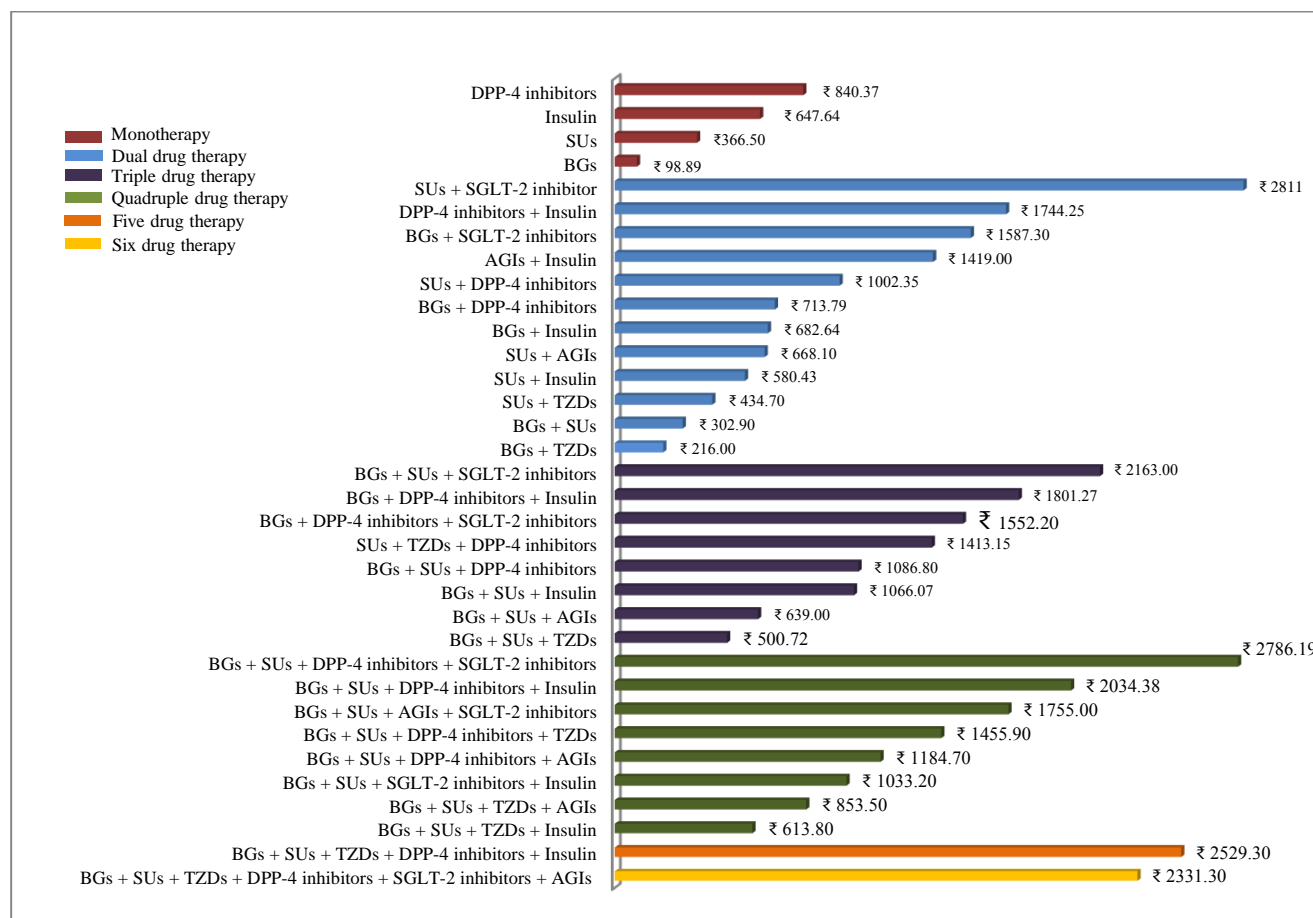


BGs: Biguanides, SUs: Sulfonylureas, DPP-4 inhibitors: Dipeptidyl peptidase-4 inhibitors, TZDs: Thiazolidinediones, SGLT-2 inhibitors: Sodium glucose co-transporter-2 inhibitors, AGIs- Alpha glucosidase inhibitors

### Figure 2: Monthly cost of therapy.

Average monthly cost was highest with DPP-4 inhibitors and least with biguanides among monotherapy. Among dual drug therapy, cost of monthly therapy was least with combined therapy with biguanides and thiazolidinediones and highest with sulfonylureas + SGLT-2 inhibitors therapy. Cost of monthly therapy for triple drug therapy was least with combination therapy of biguanides, sulfonylureas with thiazolidinediones and was highest with combination of biguanides, sulfonylureas with SGLT-2 inhibitors.

Combination therapy with biguanides, sulfonylureas, thiazolidinediones and insulin was least expensive therapy whereas combined therapy with biguanides, sulfonylureas, SGLT-2 inhibitors with DPP4 inhibitors was the costliest treatment among quadruple drug combination therapy. Combined therapy with FDC (metformin + glimepiride + pioglitazone) + sitagliptin + premixed insulin (isophane insulin + soluble insulin) was only prescribed among five drug therapy. Monthly cost for this therapy was ₹ 2529.30. Among six drug therapy, combination of FDC (metformin + glimepiride), pioglitazone, teneligliptin, empagliflozin, FDC (metformin + voglibose) was only prescribed and monthly cost of this therapy was ₹ 2331.30.

## DISCUSSION

This study showed that DM was more commonly seen in females (53.3%) as compared to males. Female predominance has been reported in previously conducted studies.[9-11] Some studies also showed deviation from above results. Study by Jain J et al, Kumar V et al, Singh A et al, showed male predominance in following percentages: 51.25%, 51%, 54.21% respectively. It could be due to this study being a cross sectional study captured data 2 days/ week.[12-14]

In this study, average number of drugs was 6.6 per prescription. The WHO proposes that optimally, this should be <2.[15,16] Possible reason for polypharmacy in diabetic patients could be because of associated comorbid conditions and complications in them.

Only 4.3% of drugs were prescribed by generic name. The percentage of drugs prescribed by generic name was extremely low considering WHO reference value of 100%.[15,16] Repeated and persuasive promotion of the proprietary products by pharmaceutical companies and demanding of innovator drugs by affluent patients for the treatment may be likely explanation for the low percentage of generic prescribing in this setting as it is a private tertiary care hospital.

Drugs from essential drug list constituted 58.9% of total prescribed drugs. Percentage of prescribed essential drugs was less as compared to studies conducted by Sharma S et al, (68.86%), Kakade A et al, (61.74%).[17,18] Ideally, all drugs should be prescribed from essential drug list.[15,16] Possible reason of less percentage of essential drugs in this study was that NLEM was not updated since 2015 and

study being conducted in tertiary care hospital, doctors usually prescribe drugs according to better efficacy or recent guidelines though newer and expensive. Such drugs may still have not found place in NLEM.

There were 37.9% of total prescribed drugs were fixed dose combinations. Drug utilization studies conducted by Kakade A et al, and Singh A et al, showed than more than half of prescribed drugs were fixed dose combinations (60% and 71.06% respectively).[14,18] Possible reason for prescribing fixed dose combinations could be that it is convenient to take one or two pills a day rather than taking several drugs with individual formulations. But in this study it is about 50% of reported in literature, it could be due to tertiary care centre where commonly drugs available as combination have already outlived their trial.

In this study, FDC of biguanides and sulfonylureas (80.10%) was the most common among prescribed fixed dose combinations followed by FDC of biguanides with DPP-4 inhibitors (14.24%). This finding was comparable to other study conducted by Venkateswara murthy N et al, which showed that FDC of metformin and glimepiride was the most commonly prescribed followed by FDC of metformin and glibenclamide.[19]

In this study, Metformin was most commonly prescribed as monotherapy in 19.47% of the prescriptions. Metformin was prescribed in combination among most commonly prescribed dual, triple, quadruple, five drug and six drug regimens. For instance, combination of biguanides with sulfonylureas and DPP-4 inhibitors was most commonly prescribed among triple drug therapy (n=81) and combination of biguanides with sulfonylureas, dipeptidyl peptidase-4 inhibitors and Insulin constitute maximum share of all drugs prescribed as quadruple drug therapy. This results were comparable with results of other studies which showed that metformin was prescribed most commonly therapy as monotherapy and as combination therapy.[19,20] Possible reason for such pattern may be that metformin has good efficacy and low cost as compared to other drugs and moreover, it is weight neutral with no risk of any hypoglycaemic episodes. Moreover, metformin is first drug to be used in accordance with NICE and ADA guidelines for the management of diabetes mellitus.[21,22]

This study showed that physicians tend to prescribe combination therapy as compared to monotherapy. Possible reason for such a pattern could be for better control of blood sugar levels and to prevent the progression of the disease.

In this study, average cost of antidiabetic drugs was ₹ 670.61/month per prescription. Minimum and maximum cost per prescription was ₹ 21.30 and ₹3847.80 per month respectively. Results of another study by Lahiry S et al, revealed that average cost per prescription was ₹ 11.24 per day. Minimum and maximum cost per prescription was ₹6.6 and 22 per day respectively.[23] Newly approved drugs in this study mainly belong to class of DPP-4 inhibitors

and SGLT-2 inhibitors which were more costlier as compared to other drugs and their addition to therapy increases cost of combined therapy.

In this study, analysis of monthly cost of therapy among drugs revealed that least expensive drug therapies were as follows: biguanides (₹98.89) among monotherapy, Combination of biguanides with thiazolidinediones (₹216 per month) among dual drug therapy, combination of biguanides with sulphonylureas and thiazolidinediones (₹500.72 per month) among three drug therapy. combination of biguanides, sulfonylureas, thiazolidinediones and insulin (₹613.80) among quadruple drug therapy. These results can be matched to study conducted by Gayathri M et al,[24] to evaluate Pharmacoeconomics of antidiabetic drugs which revealed that among monotherapy, lowest annual cost was spent by patients taking biguanides (₹840). Among annual treatment for dual drug combination therapy, lowest and highest annual cost was with combination of biguanide with thiazolidinediones (₹1935) and biguanides with DPP-4 inhibitors (₹28,025). Annual treatment of cost for triple drug combination therapy was least with combination of biguanide plus sulfonylurea plus thiazolidinedione (₹3066) whereas among annual treatment for 4-drug combination therapy, lowest annual cost was with combination of biguanide plus thiazolidinediones plus alpha glucosidase inhibitor plus sulfonylureas (₹6504).

## CONCLUSION

Drug prescribing pattern and pharmacoeconomic analysis of drugs form an important part of drug utilization studies. These studies provide feedback to physicians and promote appropriate use of drugs. Rational and cost effective medical care are the most important factors in determining healthcare delivery.

This study revealed that there is more inclination towards prescribing combination therapy as compared to monotherapy. Biguanides were most commonly prescribed among monotherapy as compared to biguanides with sulfonylureas among combination therapy and treatment with these drugs are economical.

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